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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,458	05/08/2001	Y. Tom Tang	PF-0636 USN	4361

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EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,458	TANG ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-42* is/are pending in the application.

4a) Of the above claim(s) *32-34 and 38-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-31 and 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *21-42* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 12, 2004 has been entered.

Claims Status

2. Claims 21-42 are pending in the instant application. Claims 21 and 30 have been amended as requested by Applicant in the Paper filed February 12, 2004.

Claims 32-34 and 38-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 21-31 and 35-37 are currently under examination.

Request for Rejoinder

3. Applicants' request for rejoinder of methods claims upon allowance of any of the claims drawn to the polypeptides of Group A is acknowledged.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 21-31 and 35-37 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility (including scope of enablement and written description), for reasons of record in the previous Office Actions, Paper No. 15, at pages 5-8, Paper No. 18, at pages 3-13 and below.

Applicants traverse the rejection and assert on pages 8- 9 of the response that the polynucleotides expressed in hematopoietic/immune, gastrointestinal, cardiovascular, and reproductive tissues, and the polypeptides encoded by the claimed polynucleotides are identified in the patent application as human cell surface receptor proteins, abbreviated as HCSRP. As such, Applicants assert that the claimed invention has numerous practical, beneficial uses in toxicology testing, drug development, and the diagnosis of disease, none of which require knowledge of how the polypeptide actually functions. Applicants assert on page 9 of the response that the similarity of the claimed polypeptide to another polypeptide of known, undisputed utility itself demonstrates utility beyond the reasonable probability require by law, and that the HCSRP-12 protein shares 84% sequence similarity with the pg120 receptor. It is further asserted that the probability that two unrelated polypeptides share more than 40% sequence homology over 70 amino acid residues is exceedingly small, and that the probability that the claimed polypeptide is related to the gp120 receptor is, accordingly, very high, and that the fact that the claimed polypeptide is a member of the C-type lectin receptor family alone

demonstrates utility, and that each of the members of this class, regardless of their particular functions, are useful, and that the claimed polypeptide also has patentable utility, regardless of its actual function, and that the law has never required a patentee to prove more. Applicants submit that in addition, there is direct proof of the utility of the claimed invention, and note the previously submitted declarations of Bedilion and Furness describing some of the practical uses of the claimed invention in gene and protein expression monitoring applications as they would have been understood at the time of the patent application.

Applicants quote from the Bedilion declaration on page 10 of the response, which states that any microarray containing SEQ ID NO: 12-encoding polynucleotides would be a more useful tool than microarrays lacking same in connection with conducting gene expression monitoring studies on proposed or actual drugs for treating cell proliferative disorders, immune system disorders, infections, and neuronal disorders for such purposes as evaluating their efficacy and toxicity. Applicants on pages 10-11 of the response also refers to the Furness Declaration, which describes, in particular, how the claimed polypeptide can be used in protein expression analysis techniques such as 2-D PAGE gels and western blots, and using the claimed invention with these techniques, persons of ordinary skill in the art can better assess, for example, the potential toxic effect of a drug candidate. This is not found to be persuasive. Regarding the merit of the argument, any new polynucleotide can be used in a microarray, and any new polypeptide can be analyzed on 2-D PAGE gels and western blots, and thus the asserted utilities of the polynucleotide and polypeptide are not specific. Also, the disclosure that HCSRP-12 is structurally related to pg120 receptor does not render the asserted utility specific, since the specification does not establish that the polynucleotide and encoded protein are expressed in any

diseased tissues in any way that is different from the way it is expressed in healthy forms of the same tissues. In other words, the specification does not disclose that HCSRP-12 is expressed in tissues having cell proliferative or immune system disorders, infections, and neuronal disorders at altered levels or forms. Thus, it is not a target for drug development, toxicology studies, or disease diagnosis. Significant further research would have to be conducted to identify diseases states which correlate with altered levels or forms of the claimed polynucleotides. Therefore, this asserted utility is also not substantial.

Applicants on pages 10-11 of the response also assert that the Patent Examiner contends that the claimed polynucleotide or polypeptide cannot be useful without precise knowledge of their biological function, and that the law has never required knowledge of the biological function to prove utility. Applicants mischaracterize the Examiner's position. It is true that the precise biological role or function of a protein or its encoding nucleic acid are not necessary for utility, however there must be at least one specific and substantial utility attributed to the claimed invention, which has not be demonstrated, and merely identifying that a protein is homologous to the gp120 receptor does not provide sufficient support for a specific and substantial or well-established utility, as discussed above. A specific and substantial utility for a protein that does not depend on knowledge of the activity of the protein would be use of the protein as a marker, for example, if the protein were expressed in a cancer cell but not normal cells. Use as a cancer marker would also be a specific and substantial utility of the encoding polynucleotide, if it were for example, detectably overexpressed in cancer but not normal tissue. No such correlations or activities have been shown for the instantly claimed receptor or polynucleotide.

Beginning at p.11 of the response, Applicants summarize case law on the utility requirement. The essential disagreement appears to be the interpretation of what constitutes a specific, substantial and credible utility, as will be explained more fully below.

Applicants argue at pages 13-18 of the response that the claimed invention has specific, substantial and real-world use by virtue of its use in toxicology testing, drug development, and disease diagnosis through gene expression profiling are practical uses that confer specific benefits to the public. Applicants state that there is no dispute that the claimed polynucleotide is a useful tool in cDNA microarrays used to perform gene expression analysis or that the claimed polypeptide is a useful tool in two-dimensional polyacrylamide gel electrophoresis analysis and western blots to monitor protein expression and assess drug toxicity. Applicants assert that such is sufficient to establish utility for the claimed polynucleotide.

On pages 13-16 of the response Applicants refer to the Bedilion declaration as explaining the many reasons why a person skilled in the art reading the Tang et al. '404 application would have understood that application to disclose the claimed polynucleotide to be useful for a number of gene expression monitoring applications, such as a probe for expression of the polynucleotide in connection with the development of drugs and the monitoring of the activity of such drugs. Specifically, Appellants quote from the Bedilion declaration that a person skilled in the art would have appreciated that a cDNA microarray that contained the SEQ ID NO: 12-encoding polynucleotides would be a more useful tool than a cDNA microarray that did not contain the polynucleotides in connection with conducting gene expression monitoring studies on proposed (or actual) drugs for treating cell proliferative disorders, immune system disorders, infections and neuronal disorders for such purposes as evaluating their efficacy and toxicity. The Bedilion

declaration discusses microarrays and Northern analysis for measuring such. This is not found to be persuasive. The instant specification does not substantiate a link between the claimed polynucleotides and any specific disorder. The specification merely discloses that the claimed polynucleotides are structurally related to other receptors, and that they are expected to be involved in neurotransmission (and thus, disorders). Many genes expressed in diseased tissues have nothing whatsoever to do with the disease and are not targets for drug development or toxicology. For example, actin and histone genes are expressed in diseased tissues; they are constitutively expressed in all tissues. These are not suitable targets for drug development or toxicology studies, since disruption of these genes would kill the patient.

At the second paragraph on page 15 Applicants state that nowhere does the Patent Examiner address the fact that, as described on pages 33 of the Tang '404 application, the claimed polynucleotides can be used as highly specific probes in for example, cDNA microarrays, and the claimed invention is not, in that regard, some random sequence whose value as a probe is speculative or would require further research to determine. This is not found to be persuasive. The use of the claimed polynucleotide in microarrays was discussed in the Office Action, Paper No. 18, at pages 8-10 , as not being a specific or substantial utility. While the examiner agrees that any polynucleotide, including the claimed polynucleotides, can be used in a cDNA microarray, such does not confer patentable utility on the claimed polynucleotides. Since any expressed polynucleotide can be used in a microarray, such a use is not specific to the claimed polynucleotides. Just as any orphan receptor can be used in an assay to screen for ligands, such does not confer patentable utility on a particular orphan receptor. Such can be done with any orphan receptor, and thus the asserted utility is not specific. Furthermore, since the

specification does not disclose a persuasive correlation between any disease or disorder and an altered level or form of the claimed polynucleotides, the results of gene expression monitoring assays would be meaningless without significant further research. Therefore, the asserted utility is also not substantial.

At p. 15 of the response, Applicants argue that, given that the claimed polynucleotide is known to be expressed, its utility as a measuring and analyzing instrument for expression levels is as indisputable as a scale's utility for measuring weight. Appellant reviews case law pertinent to the patentable utility of research tools. This is not found to be persuasive. Appellant's analogy is misplaced. It is true that a scale has patentable utility as a research tool. However, the object being weighed on the scale does not necessarily have patentable utility. In the instant case, microarray technology has patentable utility. However, the microarray is not being claimed, but rather a polynucleotide that can be used in microarrays. The claimed polynucleotide is not disclosed as being expressed at an altered level or form in any diseased tissue as compared to the corresponding healthy tissue. Therefore, the assertion that the claimed polynucleotide has patentable utility as a probe in, or member of, a microarray is not specific. Any orphan polynucleotide can be used in the same way.

Applicants assert that the Bedilion Declaration shows that a number of pre-March 8, 1999 publications further establish the utility of cDNA microarrays in a wide range of drug development expression monitoring applications at the time the Tang et al. '404 application was filed, and that the Brown and Shalon U. S. Patent No. 5,807,522 shows that the Patent Office recognizes the patentable utility of the cDNA technology developed in the early to mid-1990's,

and that the Rockett et al. and Lahskari et al. publications describing the state of the art further confirm the claimed invention's utility.

At pages 17-18 of the response, Applicants assert that in his declaration, Mr. Furness explains the many reasons why a person skilled in the art who read the Tang et al. '404 application on March 8, 1999, would have understood that application to disclose the claimed polypeptide to be useful for a number of gene and protein expression monitoring applications, *e.g.*, in 2-D PAGE technologies, in connection with the development of drugs and the monitoring of the activity of such drugs. Applicants assert that since the early 1990's, 2-D PAGE has been used to create maps showing the differential expression of proteins in different cell types or in similar cell types in response to drugs and potential toxic agents, and that by comparing a map of cells treated with a potential drug candidate to a map of cells not treated with the candidate, for example, the potential toxicity of a drug can be assessed. Mr. Furness explains that persons skilled in the art would appreciate that a 2-D PAGE map that utilized the SEQ ID NO: 12 polypeptide sequence would be a more useful tool that a 2-D PAGE map that did not utilize this protein sequence in connection with conducting protein expression monitoring studies on proposed (or actual) drugs for treating cell proliferative disorders, immune system disorders, infections, and neuronal disorders for such purposes as evaluating their efficacy and toxicity.

Applicants' arguments have been fully considered but are not deemed persuasive. There is no doubt that 2-D PAGE is an extremely valuable technique to analyze differential protein expression and useful to deteremine the potential toxicity of a drug. There is also no doubt that using such technologies is very useful in discovering genes associated with diseases, or in drug discovery or toxicology testing. However, the claims are not drawn to the techniques. The

claims are directed to polynucleotides and polypeptides which have not been disclosed as being associated with any particular disease or condition by its being expressed at an altered level or form in diseased tissue as compared to the corresponding healthy tissue. Any such protein can be analyzed on a 2-D PAGE. Thus, this asserted utility is not specific. Determining the relationship between the claimed polynucleotides and any specific disease or disorder would require significant further research. Therefore, this asserted utility is also not substantial.

On pages 18-20, Applicants assert that the use of nucleic acids coding for proteins expressed by humans as tools for toxicology testing, drug discovery, and the diagnosis of disease is now "well-established", and that toxicology testing in now standard practice in the pharmaceutical industry. Each of these uses will be addressed individually, because the facts and issues directed to each use are distinct and separable. First, Applicants argue that toxicology testing is a well-established utility and concludes that the claimed polynucleotides could be used in this manner and that the claimed invention possesses utility, as described by Bedilion and Furness, in their declarations, and cite a section on page 656 of the Rockett Declaration which explains that early identification of toxic drug candidates can shorten the development process and contribute substantially to the safety assessment of new drugs. Appellants also present two references, Nuwaysir et al., and Steiner and Anderson, that teach the same, and cite Nuwaysir which describes a Human ToxChip containing 2089 human clones which were selected for their well-documented involvement in basic cellular processes as well as their responses to different types of toxic insult. On page 19 of the response Applicants argue that the more genes that are available for use in toxicology testing, the more powerful the technique and cite from Rockett and Dix (reference 4) that "Arrays are at their most powerful when they contain the entire

genome of the species they are being used to study." Appellants also present an email from the primary investigator on the Nuwaysir paper, Dr. Cynthia Afshari, to an Incyte employee, dated July 3, 2000, was well as the original message to which she was responding, indicating that even the expression of carefully selected control genes can be altered. Applicants also argue that there is no expressed gene which is irrelevant to screening for toxicological effects, and all expressed genes have a utility for toxicological screening. The email of Dr. Afshari would seem to indicate that Dr. Afshari is in the process of designing chips to be used in toxicology screens, and is performing substantially more characterization of the expression patterns of candidate sequences than is disclosed in the specification at hand. Thus, the e-mail would seem to indicate that while the nucleic acid of SEQ ID NO: 12 might be useful in a toxicology chip such as those allegedly designed by Ms. Afshari, it would require substantial further research to determine such. Utility must be in readily available form, and utility of SEQ ID NO: 12 in a toxicology screen does not appear to meet that burden. See Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct,.1966).

Applicants also state that the more genes that are available for use in toxicology testing, the more powerful the technique, and that the potential benefit to the public in terms of lives saved and reduced health costs, are enormous. Applicants provide evidence of the benefits of this information on pages 21-23, in which CV Therapeutics, an Incyte collaborator, was able to use Incyte gene expression technology and other information to identify the key gene associated with Tangiers disease, and state that other customers have reduced the time associated with target discovery and validation, and that over 50 percent of the drug targets in its current pipeline of another customer were derived from the Incyte database.

Applicants' arguments have been fully considered but are not deemed persuasive.

There is no doubt that cDNA microarray technology is an extremely valuable technique in gene expression monitoring, toxicology testing, and drug efficacy testing. The same is true for 2-D PAGE. There is also no doubt that using such databases and technologies is very useful in discovering genes associated with diseases, or in drug discovery or toxicology testing. However, the claims are not drawn to the databases and techniques. The claims are directed to polynucleotides and polypeptides which have not been disclosed as being associated with any particular disease or condition by its being expressed at an altered level or form in diseased tissue as compared to the corresponding healthy tissue. Any such polynucleotide could be added to a microarray, and any such protein can be analyzed on a 2-D PAGE. Thus, this asserted utility is not specific. Determining the relationship between the claimed polynucleotides and any specific disease or disorder would require significant further research. Therefore, this asserted utility is also not substantial. In the absence of any disclosed relationship between the claimed polynucleotide or the protein that is encoded thereby and any disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

Applicants on pages 20-22 argue that there is a substantial likelihood that the claimed HCSRP is functionally related to the pg120 receptor, a polypeptide of undisputed utility, so there is by implication a substantial likelihood that the claimed polypeptide and the polynucleotide that encodes it are similarly useful, and Applicants need not show any more to demonstrate utility (*In*

re Brana). and that the HCSRP-12 protein shares 86% sequence similarity with the pg120 receptor. It is further asserted that the probability that two unrelated polypeptides share more than 40% sequence homology over 70 amino acid residues is exceedingly small, and that the probability that the claimed polypeptide is related to the gp120 receptor is, accordingly, very high, and that the fact that the claimed polypeptide is a member of the C-type lectin receptor family alone demonstrates utility, and that each of the members of this class, regardless of their particular functions, are useful, and that the claimed polypeptide also has patentable utility, regardless of its actual function, and that the law has never required a patentee to prove more. Applicants cite In re Brana, and cite the enclosed references of Curtis et al., Turville et al., Bashirova et al. and Alvarez et al., which teach that the receptors identified as human L-SIGN and human DC-SIGN bind gp120, are present on dendritic cells and bind Ebola virus. Applicants submit Exhibit B, which shows a BLAST analysis of SEQ ID NO: 12 and human L-SIGN and human mDC-SIGN type I isoform. The analysis shows that with a few sequence insertions, the two receptors share 99.7% identity with SEQ ID NO: 12, which corroborates the original determination of the instant application that HCSRP-12 was correctly assigned to the class of receptors that bind to HIV envelope glycoprotein pg120. Applicants also submit Exhibit C and D, which show a C-type lectin domain in the protein of SEQ ID NO: 12. Applicants assert that is was known in the art at the time the application was filed that C-lectin receptors such as the pg120 receptor could be useful for detection of virus, inhibition of viral infection, and for development of vaccines, and that because of the relationship between the gp120 receptor and C-lectin receptor proteins as a class, persons skilled in the art at the time the

application was filed would have considered HCSRP-12 to be an important and valuable tool for use in research on cell proliferative disorders, immune system disorders, and neuronal disorders.

Applicants' arguments have been fully considered but are not deemed persuasive. It is not disputed that the protein of the instant invention is a receptor in the pg120 receptor C-lectin receptor family. However, the specification only refers to the activities or functions of all of the proteins disclosed in the specification as a group, and does not point to any activity or function that would be specific for the claimed protein of SEQ ID NO: 12. If the specification would have asserted a utility based on the high homology to other lectin-like receptors that bind viruses, that could have been a specific and substantial utility. However, the only reference to this is in Table three, sixth column, heading Homologous Sequences, which identifies Non-CD4 glycoprotein gp120 receptor GENESEQ AAR32188 as being homologous to the protein of SEQ ID NO: 12. Merely identifying that a protein is homologous to the gp120 receptor does not provide sufficient support for a specific and substantial or well-established utility.

On pages 22-23, Applicants assert that over the past several years, a vibrant market has developed for databases containing all expressed genes, and that the databases sold by Applicants' assignee, Incyte, include exactly the kinds of information made possible by the claimed invention, such as tissue and disease associations, and that such databases have proven to be valuable in, for example, the identification and development of drug candidates, and therefore the instant invention has commercial success and demonstrates utility.

Applicant's argument has been considered but is not found persuasive. The case law indicates that a rejection under 35 U.S.C. § 101 *for lack of operability* can be overcome by a showing of actual use or commercial success. The instant issue is whether or not the asserted

utilities meet the three-pronged test for credibility, specificity, and substantiality. Such is not necessarily addressed by a showing of commercial success or actual use. The databases sold are valuable to the scientific community because of the **potential** importance of the encoded proteins in various diseases or assays. The proteins in these cases are being used to discover what their biological significance is, and the use of a protein, or the DNA encoding it, to discover what its properties or uses are or to discover what proteins or molecules bind to it, does not constitute a specific, substantial or well-established utility, and is an invitation to experiment. If **this** specific receptor were sold because of the specific properties that the receptor possessed, this may be evidence of commercial success and utility. The selling of databases containing the instantly claimed invention is not evidence that the claimed invention has actually been used or enjoys commercial success, because the databases also contain hundreds or thousands of nucleic acids.

On pages 23-26 Applicants argue that the precise biological role or function of an expressed polynucleotide or polypeptide is not required to demonstrate utility, that a "unique" or "particular" utility has never been required by law, and cites the PTO Utility Guidelines (66 F.R. at 1095), and that membership in a general class is insufficient to demonstrate utility only if the class contains a sufficient number of useless members such that a person of ordinary skill in the art could not impute utility by a substantial likelihood, and that as the C-type lectin receptor family is sufficiently specific to rule out any reasonable possibility that HCSRP-12 encoded by the claimed polynucleotides is useful.

Applicant's arguments have been considered but are not found persuasive. It is true that the precise biological role or function of a protein or its encoding nucleic acid are not necessary for utility, however there must be at least one specific and substantial utility attributed to the

claimed invention, which has not be demonstrated, and merely identifying that a protein is homologous to the gp120 receptor does not provide sufficient support for a specific and substantial or well-established utility, as discussed above. It is not a requirement that the polypeptide have a completely unique activity in order to have a patentable utility. For example, all DNA ligases ligate the same substrate, DNA, and these proteins all have a patentable utility even though they are not completely unique in at least one activity. However, at least one specific and substantial activity must be disclosed. A specific and substantial utility for a protein that does not depend on knowledge of the activity of the protein would be use of the protein as a marker, for example, if the protein were expressed in a cancer cell but not normal cells. No such correlations or activities have been shown for the instantly claimed receptor.

At p. 26-28 of the response, Applicants argue that the rejection is incorrectly based on the grounds that the use of an invention as a tool for research is not a substantial use. Applicants urge that only a limited subset of research uses are not substantial: those in which the only known use for the claimed invention is to be an object of further study, thus merely inviting further research. This is not found to be persuasive. As discussed above, whereas a scale or a microarray or a gas chromatograph has patentable utility as a research tool, the objects being evaluated with those research tools do not necessarily have patentable utility. In the instant case, the claimed polypeptide is not disclosed as having a specific activity, as opposed to a DNA ligase, which does have a specific activity, or having any property that can be specifically useful. The claimed invention is, in fact, the object of further study, merely inviting further research.

Beginning at p. 28 of the response, Applicants challenge the legality of the Patent Examination Utility Guidelines. In response, an Examiner has no authority to comment on the legality of the Guidelines.

Therefore, for the reasons discussed in the Office Actions, Paper No. 15 and Paper No. 18 and above, the rejection based on 35 U.S.C. § 101 is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5.1 Claims 21-31 and 35-37 also remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention, for reasons of record in the previous office action, and above. Even if the specification were enabling of how to use the HCSRP-12 nucleic acid or polypeptide, enablement would not be found commensurate in scope with the claims. If one of skill in the art does not know how to use the nucleic acids or proteins the skilled artisan would clearly not know how to use nucleic acids encoding and polypeptides that are 85% identical to the amino acid sequence of SEQ ID NO: 12 or fragments of SEQ ID NO: 12, or polynucleotides 85% identical to the polynucleotide of SEQ ID NO: 25.

5.2 Claims 21, 23, 26, 27, 28, 30, 35 and 37 also remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention, for reasons of record in the previous office actions, Paper No. 15 at pages 8-10 and Paper No. 18, at pages 14-15, and below.

Applicants traverse the rejection on pages 30-35 and assert the requirements necessary to fulfill the written description requirement of 35 U.S.C. § 112, first paragraph, are well established by case law, and cite *Vas-Cath Inc. v. Muhurkar,* in which the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, in which the invention is, for purposes of the "written description requirement", whatever is now claimed. Applicants also draw attention to the Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, first paragraph, "Written Description", in which an applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

Applicants assert that SEQ ID NOS: 12 and 25 are specifically disclosed in the application and variants are disclosed, and that the specification provides an adequate written description of the recited polynucleotide and polypeptide sequences.

Applicants assert that the Examiner's position that the subject matter is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is believed to present a misapplication of the law. On page 32, Applicants cite *Fiers v. Revel*, and

argue that if a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, then a description also requires that degree of specificity. Applicants on pages 32-33 cite *University of California v. Eli Lilly and Co.,* and *Lilly*, and submit that in those cases, nucleic acids that were defined on the basis of potential methods of isolating DNA or functional characteristics did not comply with the written description requirement of 35 U.S.C. § 112, first paragraph, and assert that the claims at issue in the present application define polynucleotides and polypeptides in terms of chemical structure, rather than functional characteristics, and therefore the claims of the subject application are fundamentally different from those found in *Lilly* and *Fiers*. Applicants assert that there is no reliance merely on a description of functional characteristics of the polynucleotides or polypeptides recited by the claims, and that by failing to base its written description inquiry "on whatever is now claimed", the Office Action failed to provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in Lilly and Fiers. These arguments are not found persuasive, because to provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof, which were considered and discussed in the analysis of the claims.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere

statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polypeptide sequence SEQ ID NO: 12 and polynucleotide of SEQ ID NO: 25, and discusses how variants may be obtained, and it cannot be established that a representative number of species have been disclosed to support the genus claim based on a single sequence.

On pages 34-35, Applicants argue that the claims at issue do not describe a genus which could be characterized as highly variant, and submit the reference of Brenner et al. as evidence illustrating that the claimed genus is of narrow scope. Brenner teaches that 30% identity is a reliable threshold for establishing evolutionary homology between sequences aligned over at least 150 residues, and that ≥40% identity over at least 70 residues is reliable in signifying homology between proteins. Applicants argue that in accordance with Brenner et al., naturally occurring molecules may exist which could be characterized as human cell surface receptor proteins and which have as little as 40% identity over at least 70 residues to SEQ ID NO: 12, and the variant language of the present claims, recite for example, polynucleotides encoding "an amino acid sequence having at least 85% sequence identity to SEQ ID NO: 12", and that this variation is far less than that of all potential human cell surface receptor proteins related to SEQ ID NO:" 12. Applicants' arguments have been fully considered but are not deemed persuasive. Only a single polynucleotide and polypeptide have been disclosed. The recited structure

combined with a functional limitation would usually provide adequate written description. However, in the instant case, having homology to the gp120 receptor does not mean that the instantly claimed protein binds gp120, and such was not disclosed in the specification.

On pages 34-35, Applicants assert that in the *Lilly* and *Fiers* cases, the parties claimed benefit of priority from 1977 and 1979, respectively, and thus the written description inquiry in those cases was based on the state of the art at essentially at the "dark ages" of recombinant DNA technology. Applicants argue that the present application has a priority date of March 8, 1999, and with the remarkable advances in recombinant DNA technology in the 20 or more years from the time of filing of the applications in *Lilly* and *Fiers*, one of skill in the art would recognize that, given the sequence information of SEQ ID NO: 12 and SEQ ID NO: 25, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed polynucleotide variants at the time of filing of this application. This is not found persuasive because although recombinant DNA technology has advanced tremendously since the time of *Lilly* and *Fiers*, the case law pertaining to written description requirement still requires that to provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus, which factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. Because the instant application only discloses one polypeptide sequence, and the claims do not recite any function, the written description has not been met.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 21-30 and 35-37 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record in the previous Office Actions, Paper No. 15, at pages 10-11, and Paper No. 18, at page 15 and below.

Applicants traverse the rejection on pages 35-37 of the response and contend that the term "naturally occurring" is a well-known term in the art which Applicants intended to be used in such context, and as such, no further definition of the term is necessary, and cite MPEP 2163 IIA39(a). On pages 36-37, Applicants assert that one of ordinary skill in the art would recognize that "a naturally occurring amino acid sequence" is one which occurs in nature, and such molecules could be identified using hybridization and/or PCR techniques, and the definition of HCSRP in the specification encompasses naturally occurring variants of SEQ ID NO: 12 from different species.

Applicants' arguments have been fully considered but are not deemed persuasive.

If claims 21 and 30 were to be read as broadly as its language allows, when read in isolation, its scope would not be clear. The specification provides no guidance that would allow those skilled in the art to determine, with a reasonable degree of confidence, whether any of the sequences that are at least 85% identical to SEQ ID NO: 12 occur naturally and, if so, which they would be. The only way to definitely fix the scope of the claims would be to compare SEQ ID NO: 12 to all naturally occurring sequences, clearly an impossible task. Thus, even if we were to

ignore the ambiguities suggested by the specification, the metes and bounds of the claim are unclear.

As the Federal Circuit recently noted,

> [t]he Supreme Court explained the reason underlying the indefiniteness doctrine 60 years ago in United Carbon Co. v. Binney & Smith Co., 317 U.S. 228, 236, 55 USPQ 381, 385 (1942):
>
> > A zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims would discourage invention only a little less than unequivocal foreclosure of the field. Moreover, the claims must be reasonably clear-cut to enable courts to determine whether novelty and invention are genuine.

Exxon Research and Eng'g Co. v. United States, 265 F.3d 1371, 1376, 60 USPQ2d 1272, 1276 (Fed. Cir. 2001). The court held that compliance with 35 U.S.C. § 112, second paragraph, is determined by "whether 'the claims at issue [are] sufficiently precise to permit a potential competitor to determine whether or not he is infringing.'" Id. (bracketed text in original, quoting Morton Int'l, Inc. v. Cardinal Chem. Co., 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993)). That test is not met here.

Since the scope of claims 21 and 30 cannot be determined, the claims are indefinite. Claims 22-29 and 35-37 depends on claim 21 and also shares its deficiency.

It is believed that all pertinent arguments have been answered.

Conclusion

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (571) 272-0871.

Official papers Before Final and After Final filed by RightFax should be directed to (703) 872-9306.

The customer service RightFax number is (703) 872-9305.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Eileen B. O'Hara, Ph.D.

Patent Examiner